Probe based laser diagnostics and optical image-guided interventions and metrology

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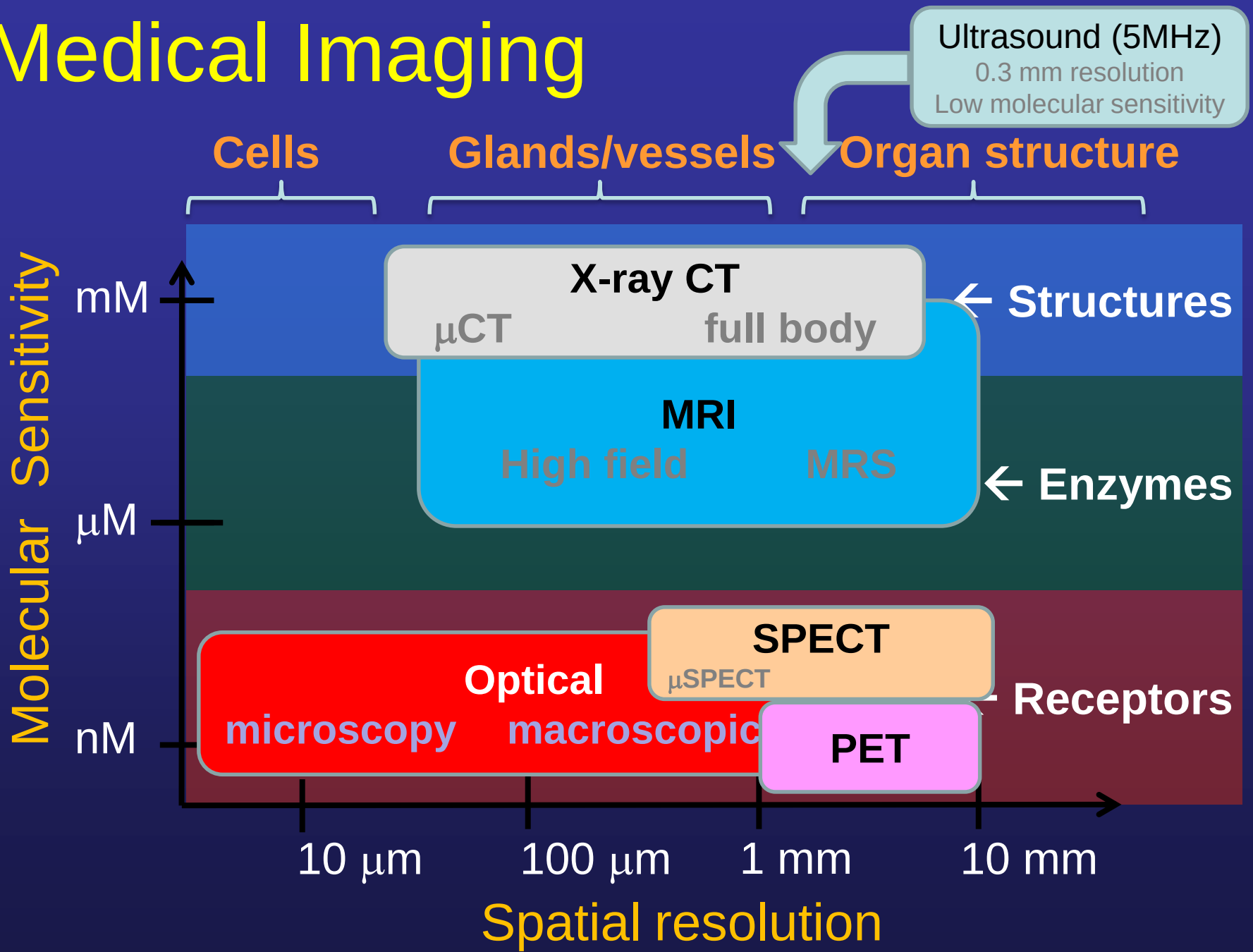
Medical Imaging



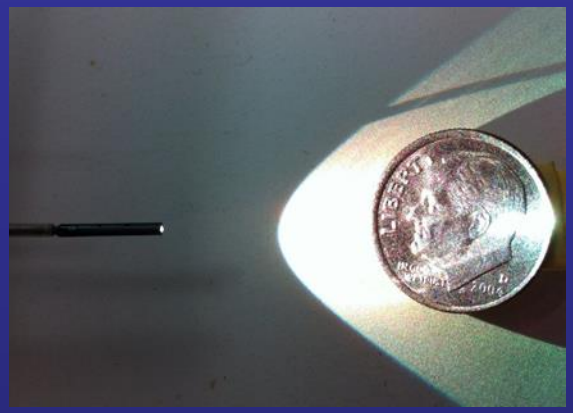
Tichauer et al., 2015

Medical Imaging Attributes

- High spatial resolution (2D and 3D)
- Several methods of molecular sensitivity
  - Reflectance
  - Fluorescence
  - Raman/CARS
  - Scattering/OCT
- Wide bandwidth allows parallel channels
- High speed – video rates
- Limited depth of penetration*
- Limited field of view*
- Small size (portable)

* Overcome by small probe-based microscopy/endoscopy and digital mosaicking

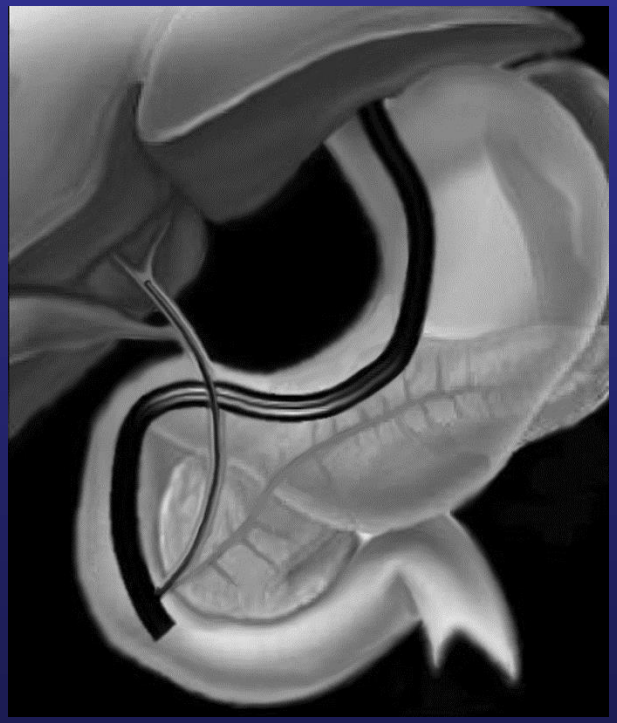
Take Home Message



Any laser-based optical imaging
used in lab microscope studies
can be packaged into the size of an earthworm
for being field deployable

Next 30 slides show how we do this for medical imaging

Problems with ultrathin & flexible endoscopes and borescopes

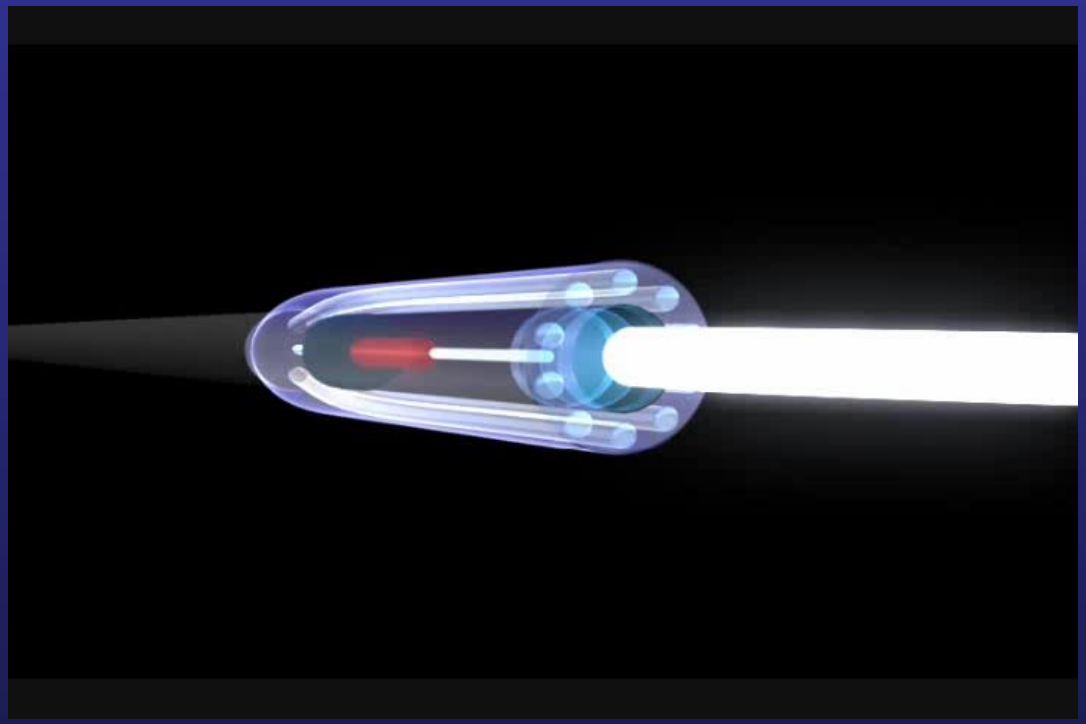


Lee, et al., 2010 J. Biophotonics

- Not high image quality
  - Not high in both resolution and field of view
- Not highly flexible
  - Fragile & Expensive
- Not integrated with laser based diagnosis & therapy

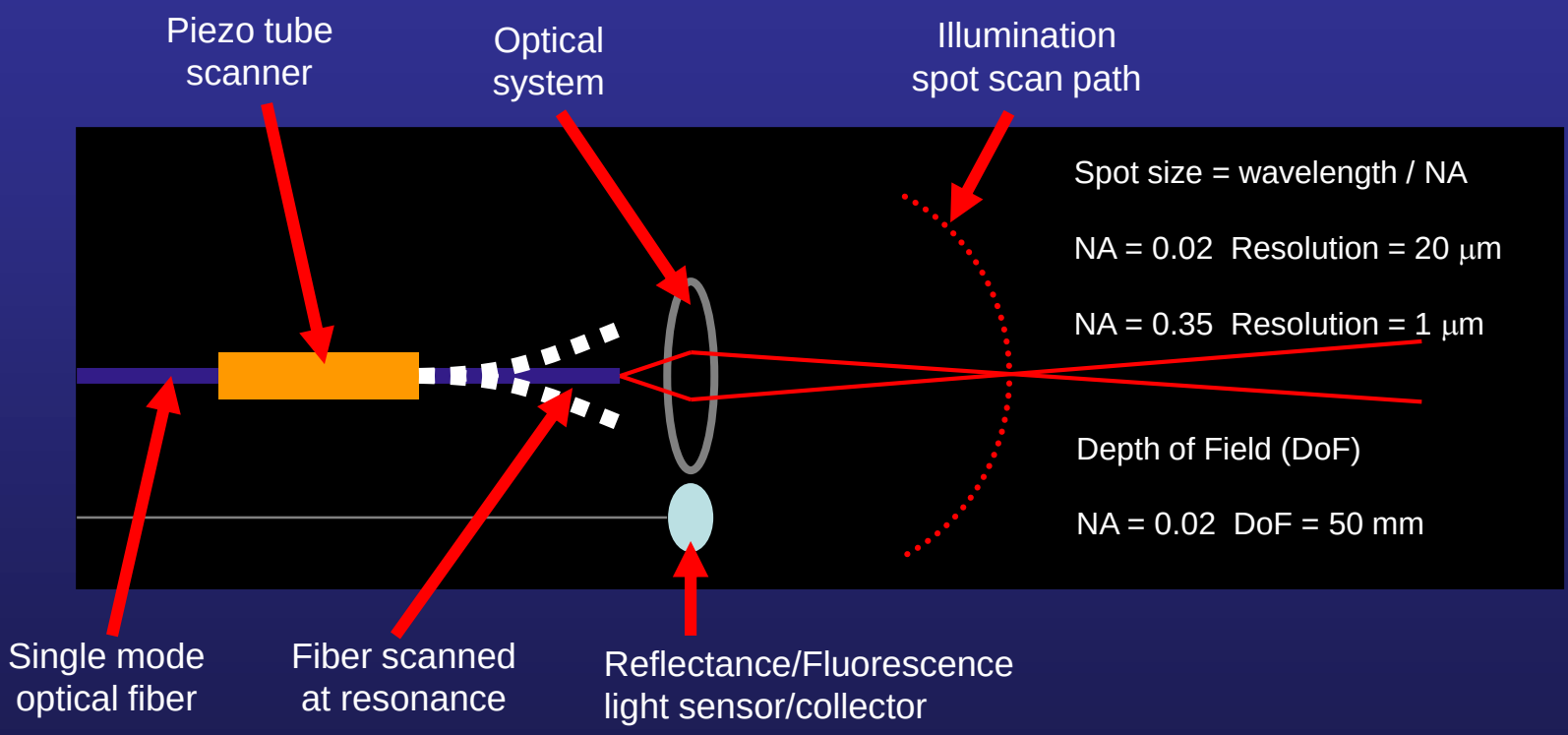
SFE Animation

Rigid tip is size of grain of rice



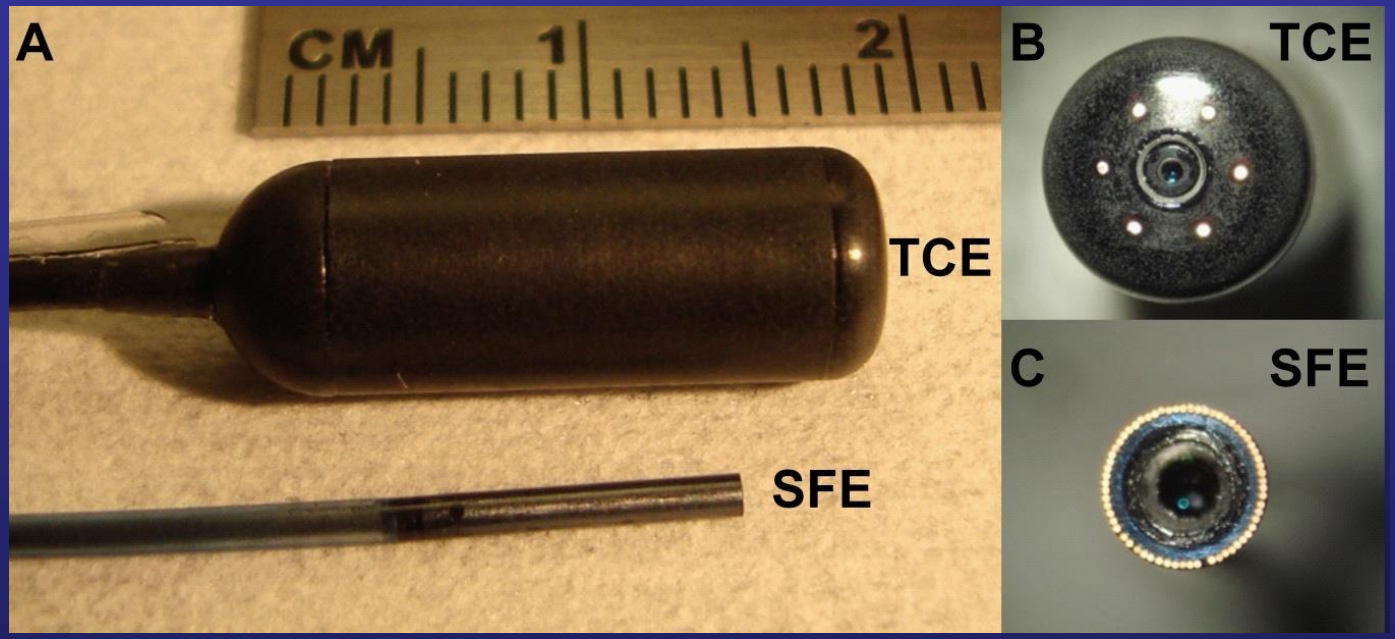
Animation by Mr. Duff Hendrickson, Seattle, WA, copyright University of Washington.

SFE Concept



SFE – Scanning Fiber Endoscope

UW Scanning Laser Endoscopes

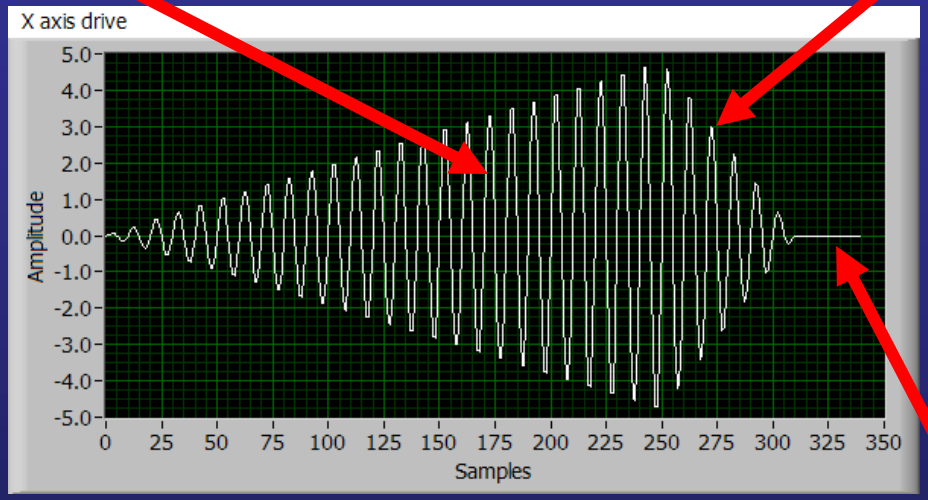


SFE – Scanning Fiber Endoscope
TCE – Tethered Capsule Endoscope
both in non-significant risk medical device studies

Scanner Drive Signal

Imaging portion of drive

Retrace portion of drive

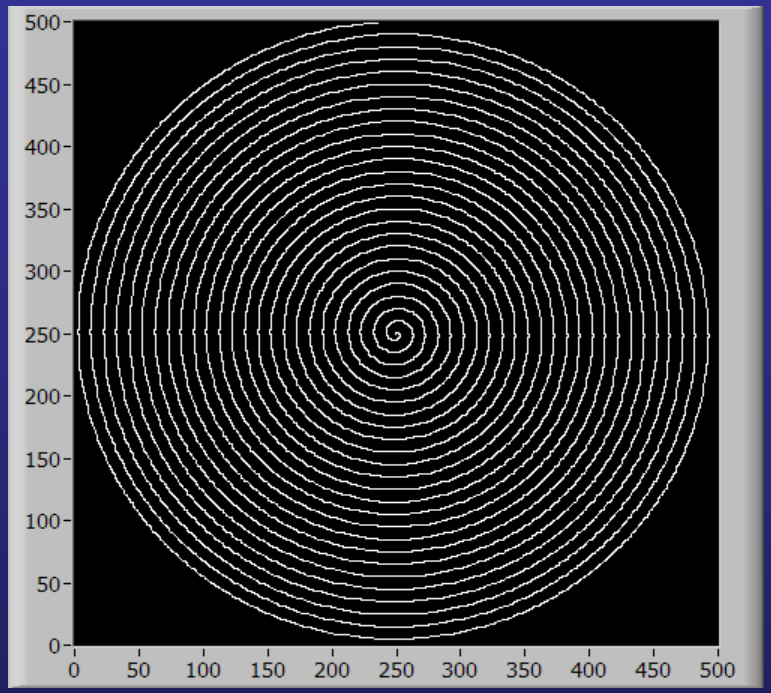


Note: fewer spirals shown for clarity

No drive, settling time

Y axis is driven 90 degrees out of phase with the X axis.
During retrace drive phase is reversed (not shown) for rapid braking.
Drive amplitude can be shaped for best image quality (during calibration).
Settling time is adjusted to achieve desired frame rate.

Spiral Scan Pattern



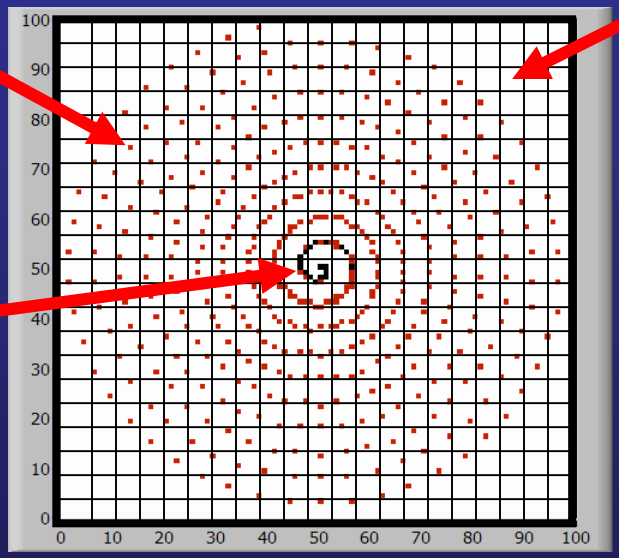
Current scanned fiber endoscopes scan in a spiral pattern starting in the center. Spiral scan frequency is ≈ 11,000 Hertz (software corrects for any deviation). 250 spirals are used to form a 500-line image leaving 83 spirals for retrace in a device with a 30 Hertz frame rate.

Mapping Spiral Scan to Pixels

Intensity sample

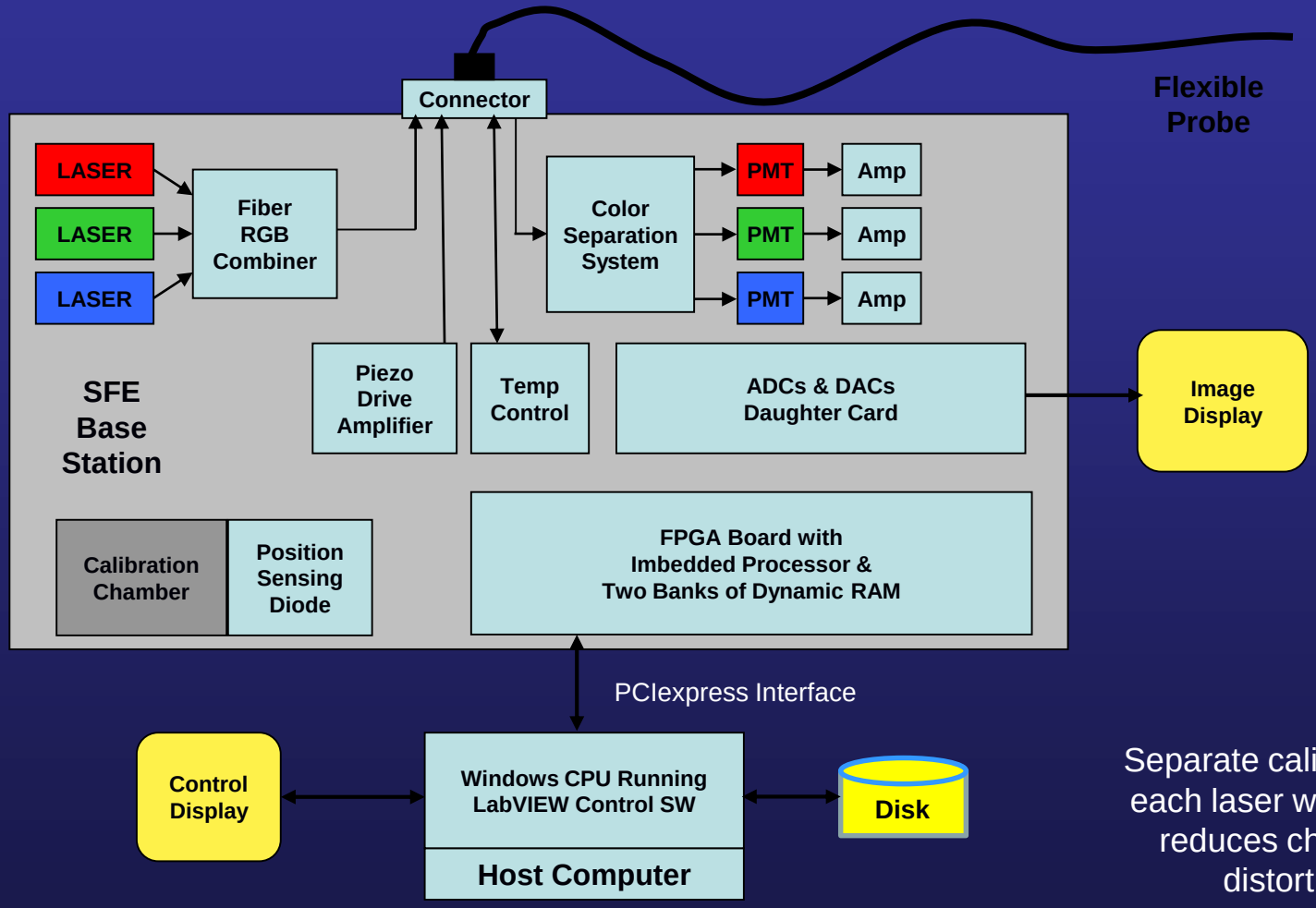
Image pixel area

In central portion of spiral multiple samples are averaged to form an image pixel



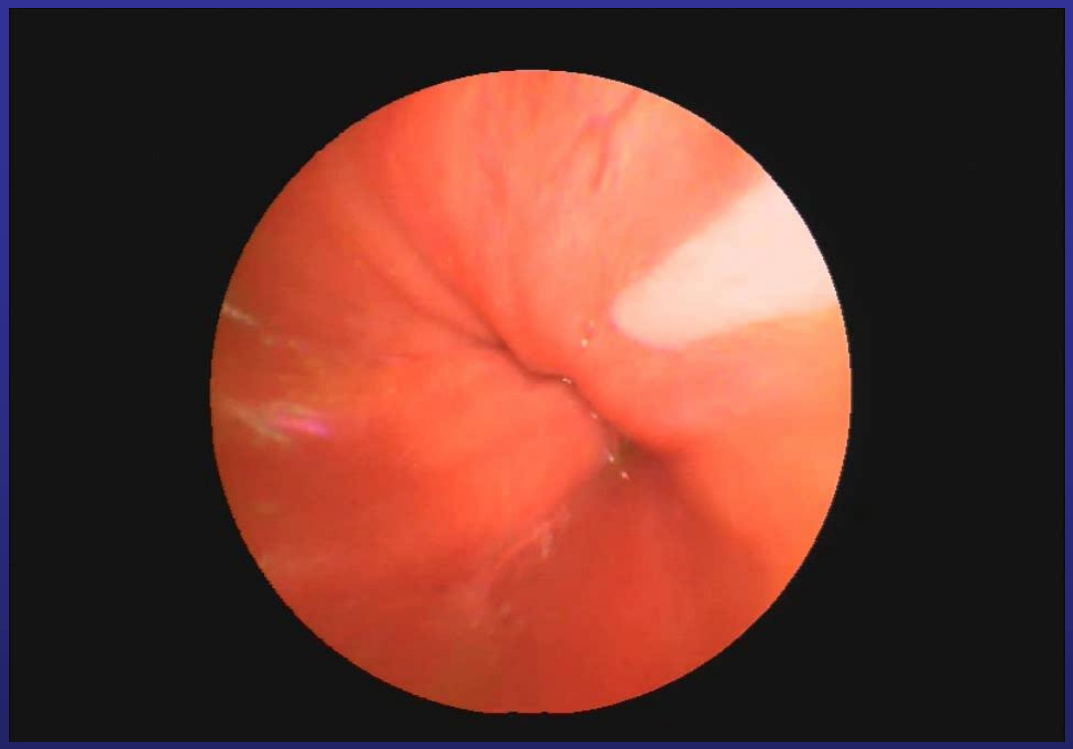
Samples are captured at a constant 25 MHz rate, oversampling the center.

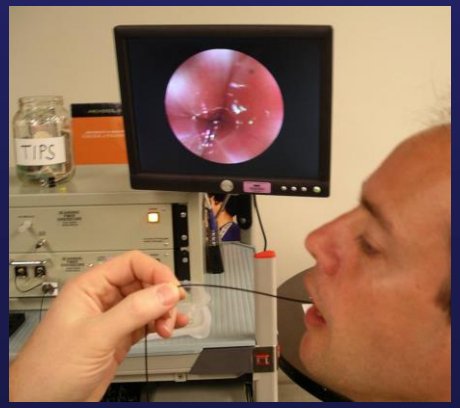
SFE System Block Diagram



Separate calibration for each laser wavelength reduces chromatic distortion.

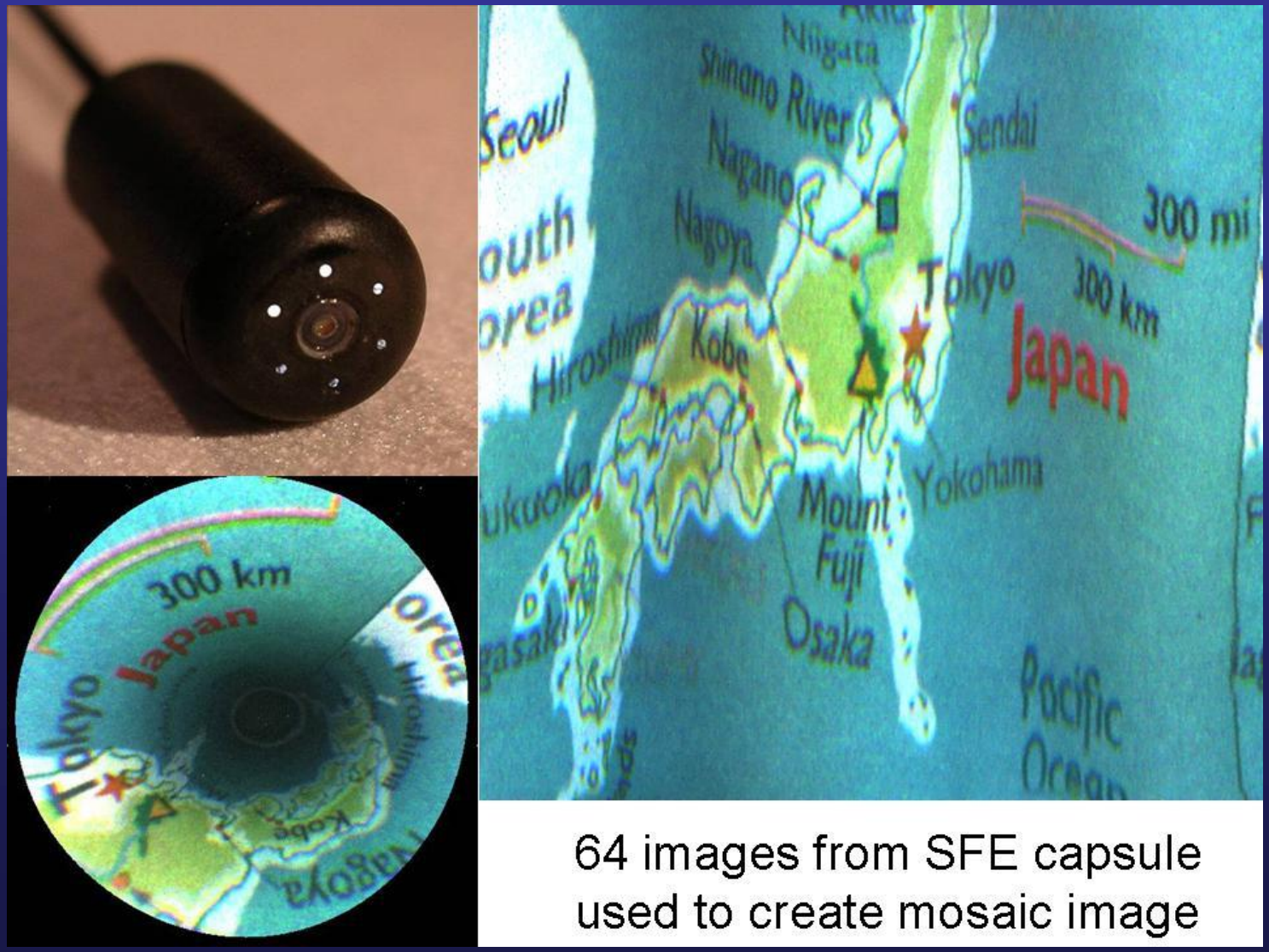
Tethered-capsule SFE imaging human subject lower esophagus





Tethered-Capsule Endoscope

Seibel et al., 2008; Carroll & Seitz, Intl. J. Computer Vision (2009)



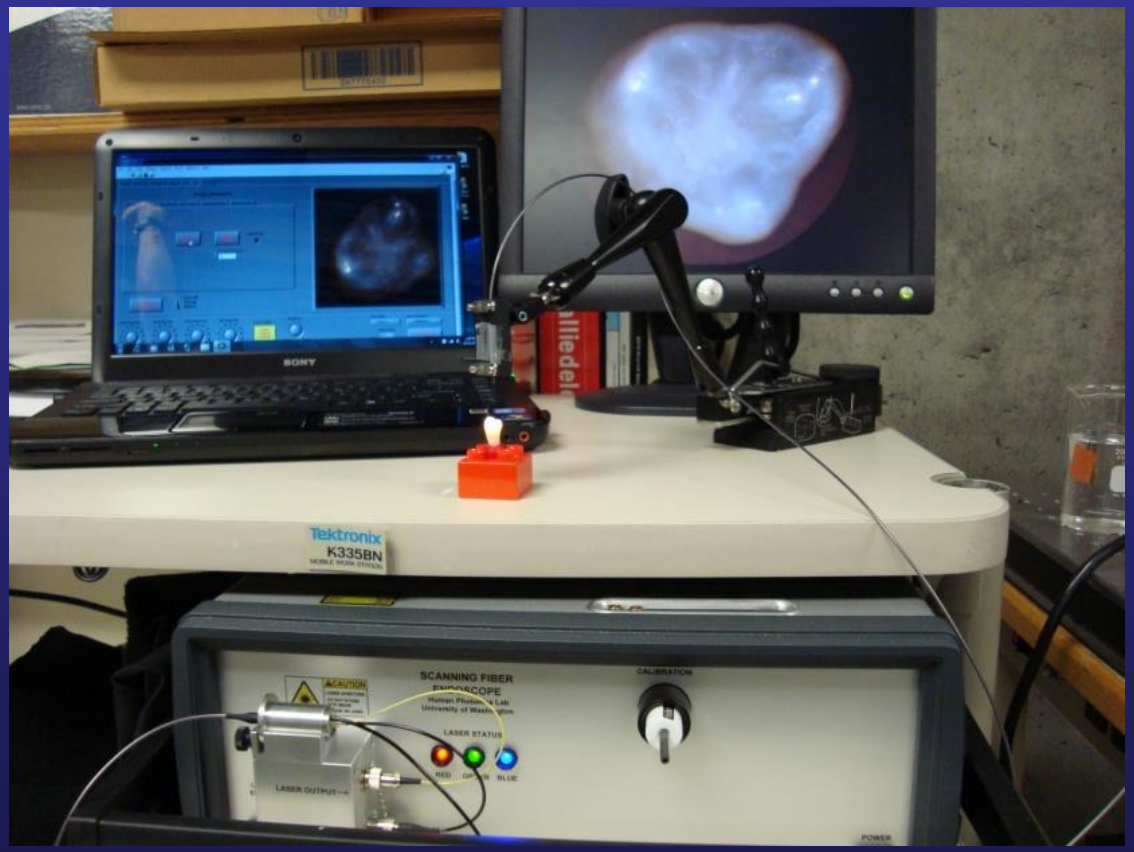
64 images from SFE capsule used to create mosaic image

1.2-mm SFE imaging

SFE in quadrant of
3.2 mm ID tube

SFE video frame showing
20 micron spatial resolution

Portable SFE System

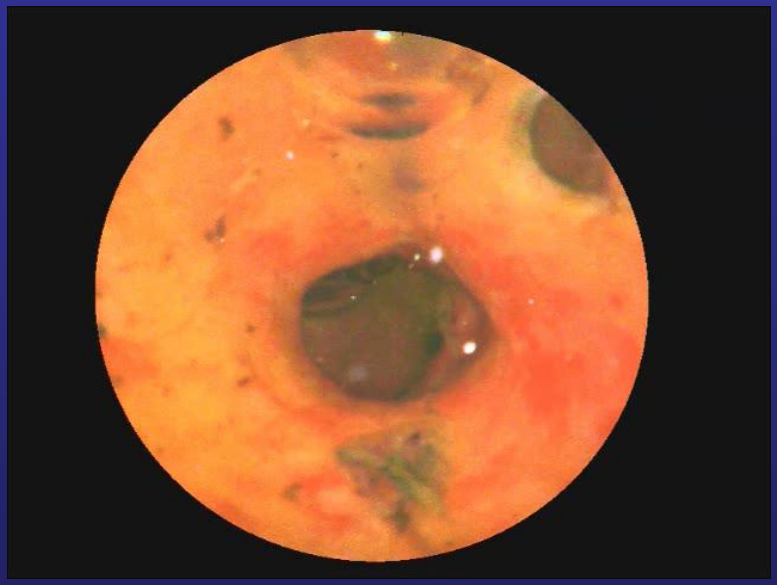


Zhang, Nelson, & Seibel, ***J. Biomed Optics***, 2011, 2012, & 2013.

Bile duct imaging

SpyGlass®, Boston Sci.*

*Complements: Dr. Anthony Bohorfoush, Seattle Gastroenterology Associates



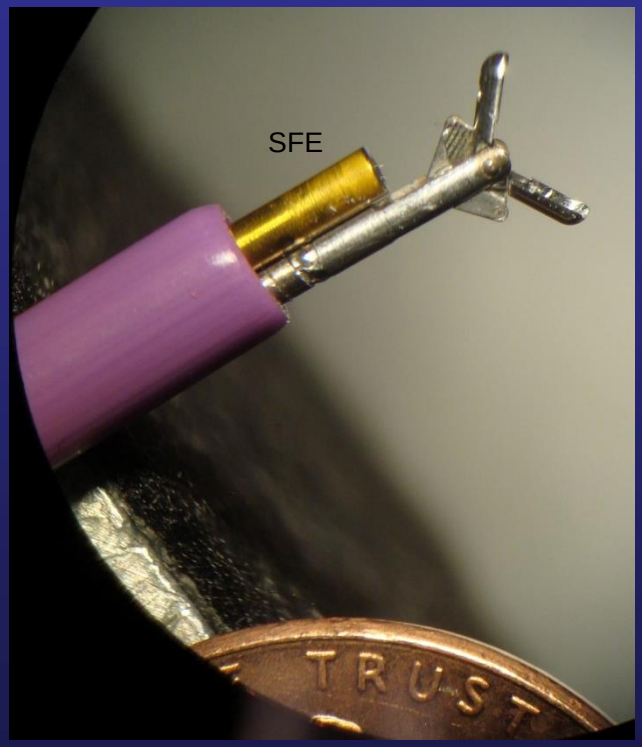
SFE third human test**

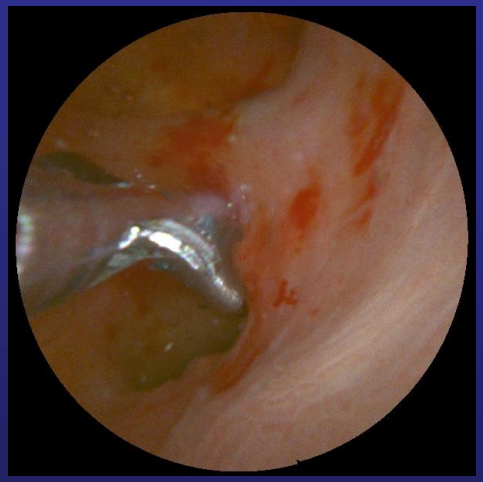
**After biliary stones and sludge were removed

Seibel et al., Proc. SPIE, 2012
Templeton et al., GIE, 2014

Delivery of Guided Interventions

Endoscopy, Pulmonology, Cystoscopy - Biopsy

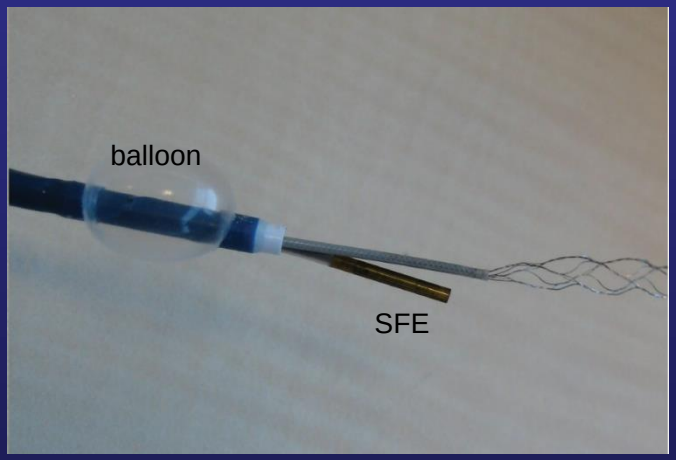




Seibel, et al., Proc. SPIE 2012
Soper et al., IEEE TBME, 2010
Soper et al., IEEE TBME, 2012

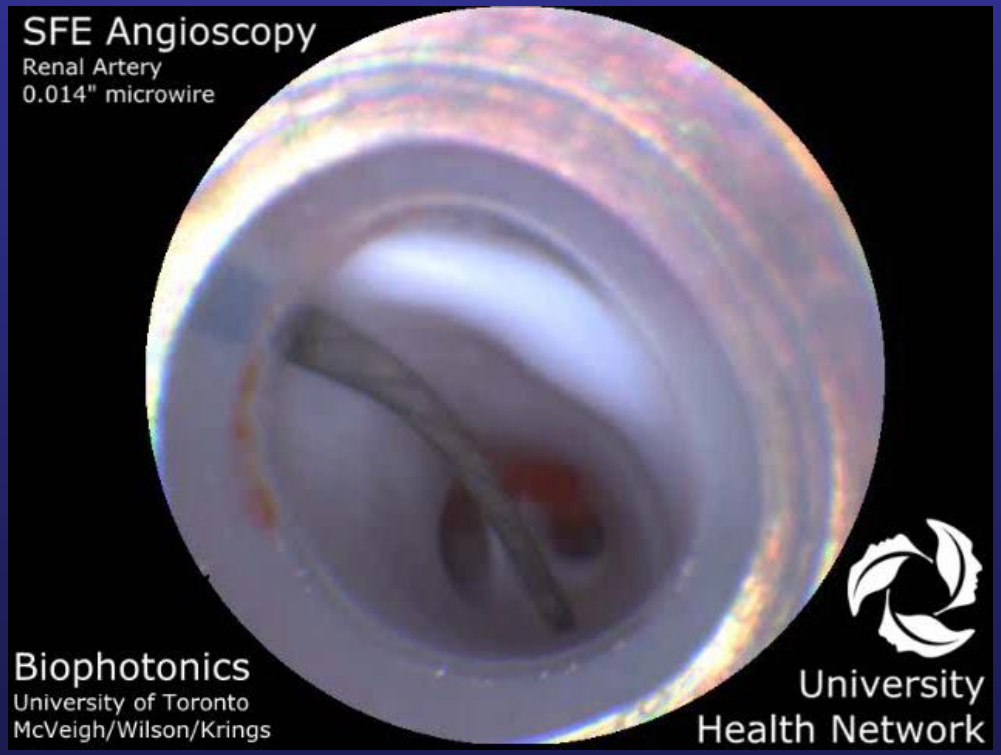
Angioscopy

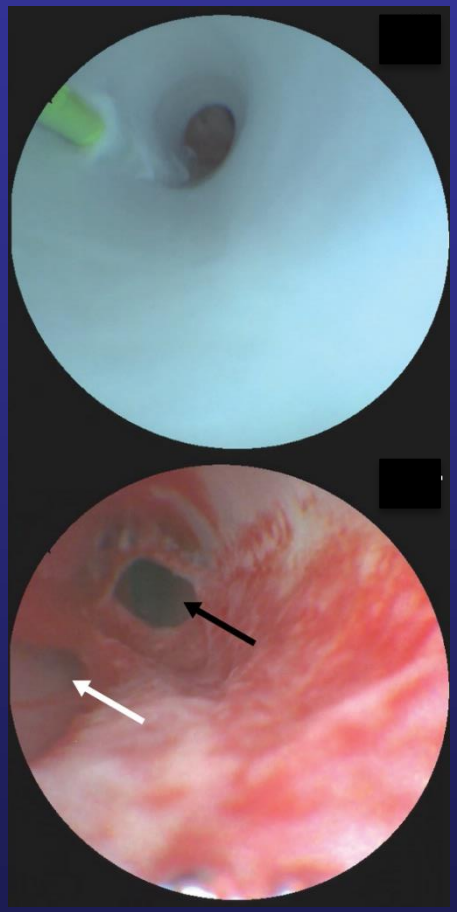
SFE with stent retractor
in balloon catheter



SFE Angioscopy of Microwire

Renal artery of live pig

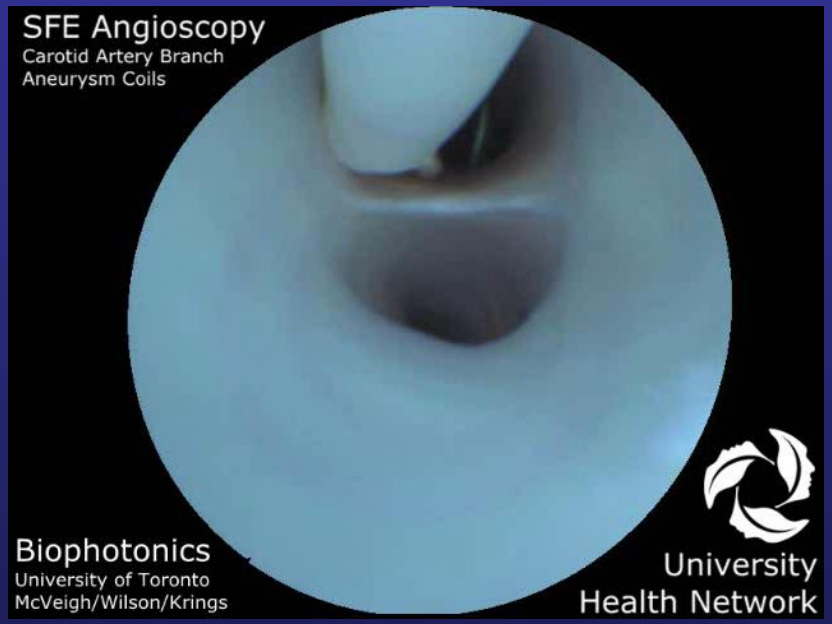




McVeigh et al., 2014

Angioscopy of Carotid Artery Interventions

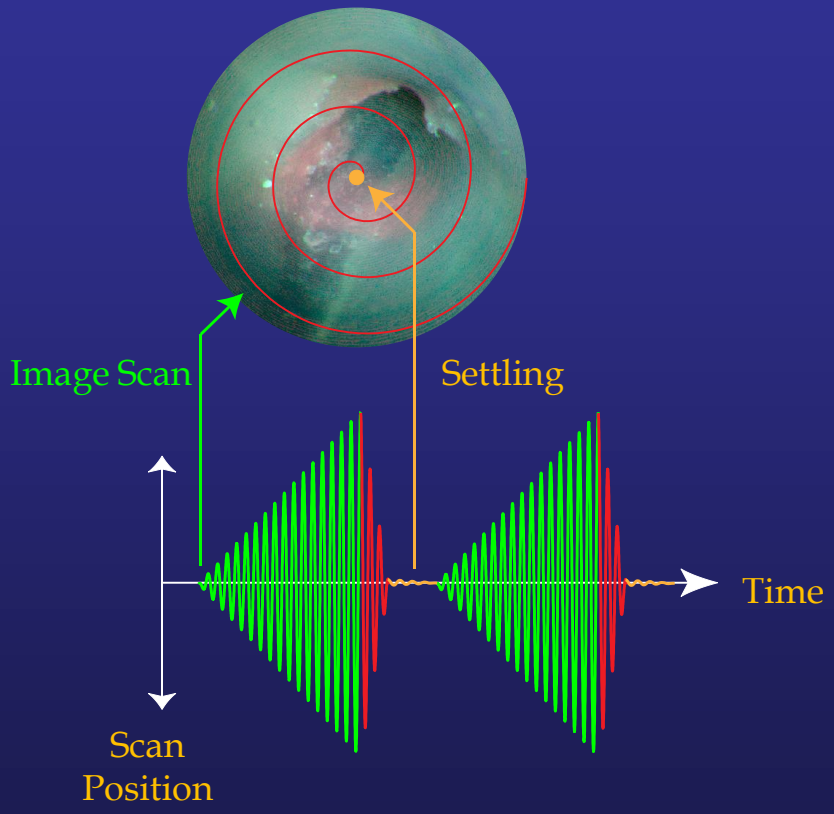
Live pig 1.5x speed

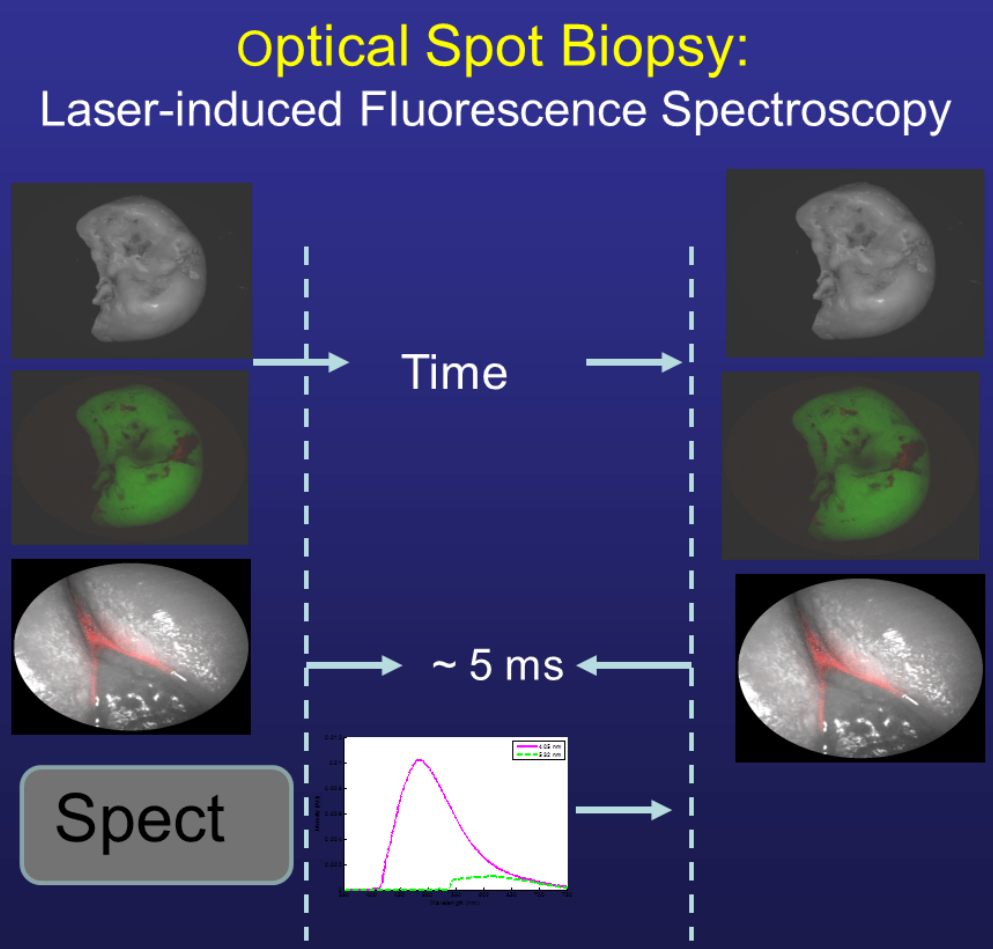


Live pig 2x speed

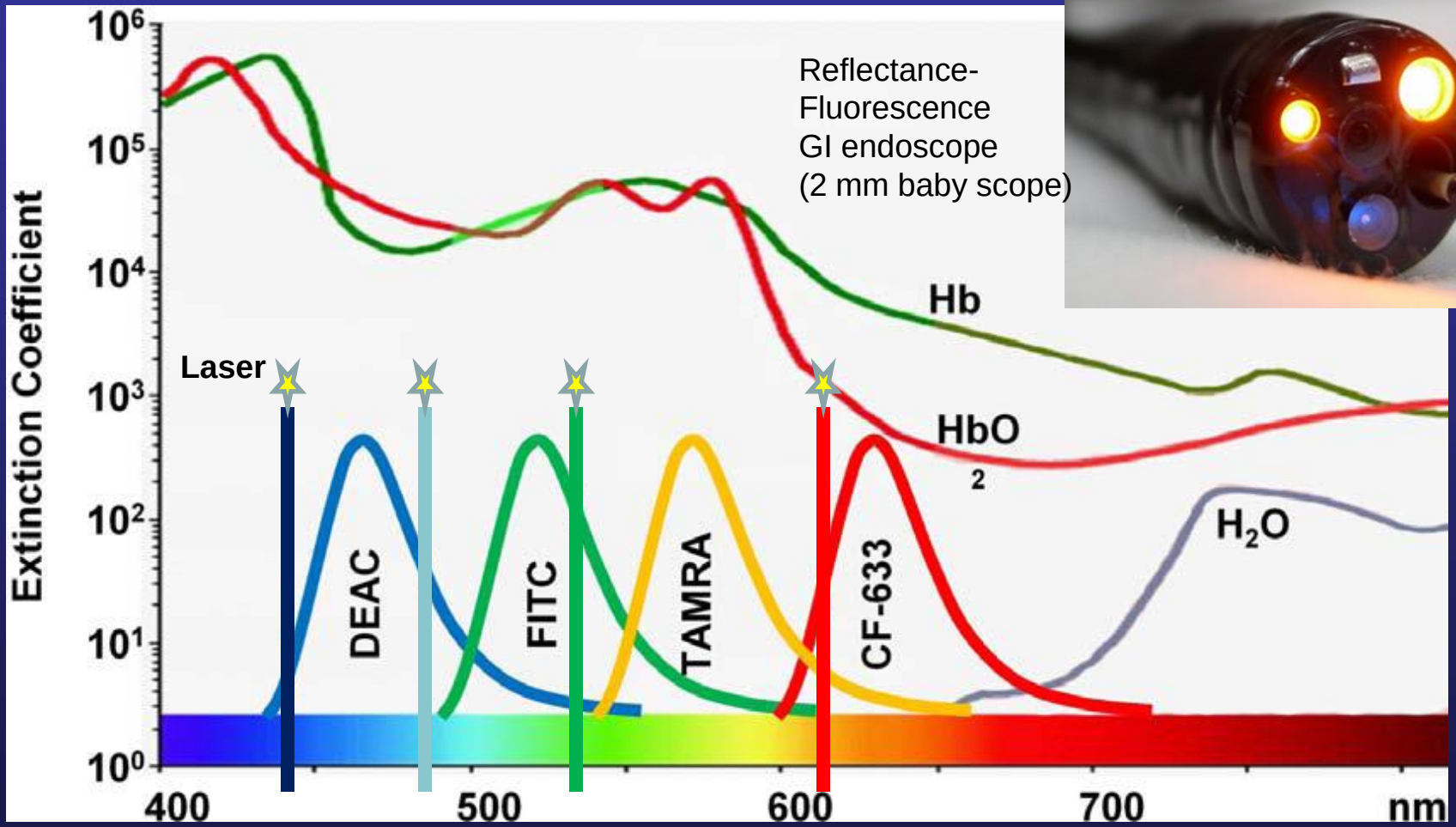
McVeigh et al., Neurosurgery 2014

Frame Sequential Fluorescence Spectroscopy





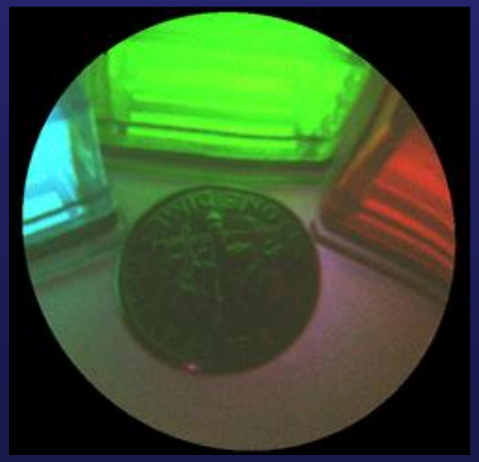
Multispectral Fluorescence Imaging



Reflectance-
Fluorescence
GI endoscope
(2 mm baby scope)

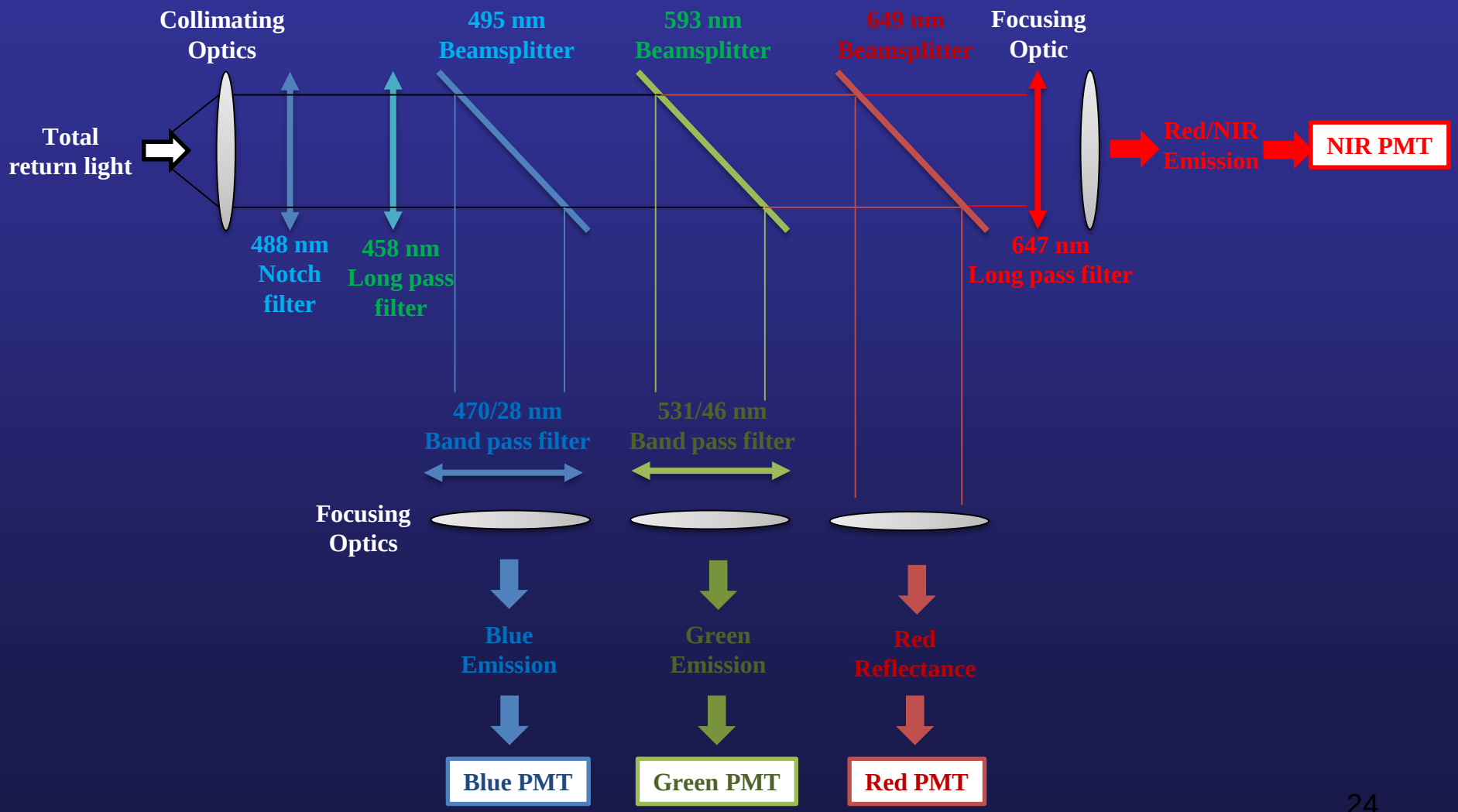
Multi-Color Fluorescence & nM Sensitivity

- 3 fluorescence channel SFE has been fabricated along with a red reflectance channel for grayscale imaging and distance compensation
- Calibration standards are used to determine 4 -10 nM sensitivity (Yang JBO, 2014)



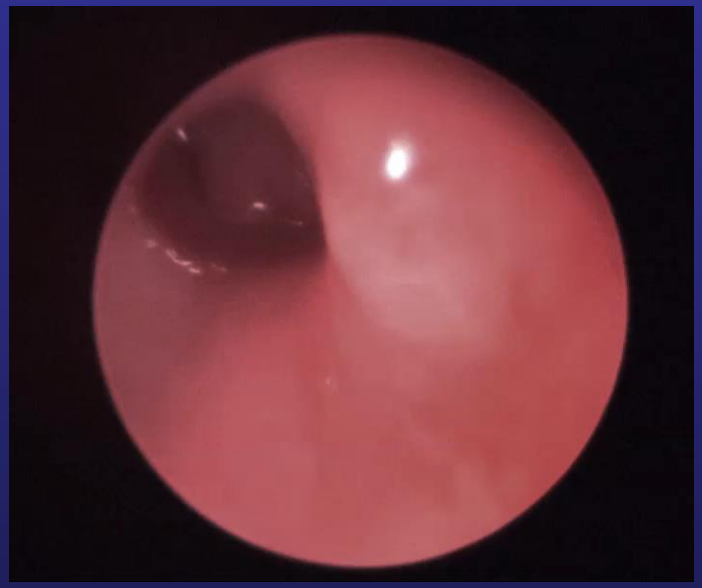
SFE Color Separation System

-- for concurrent multi-channel detection: 3 fluorescence, 1 reflectance

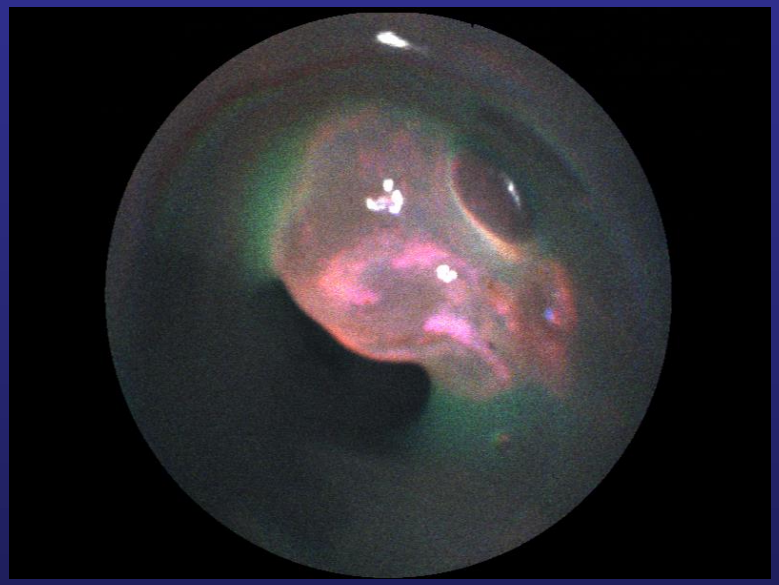


Multispectral SFE (in vivo mouse colon)

White light reflectance imaging



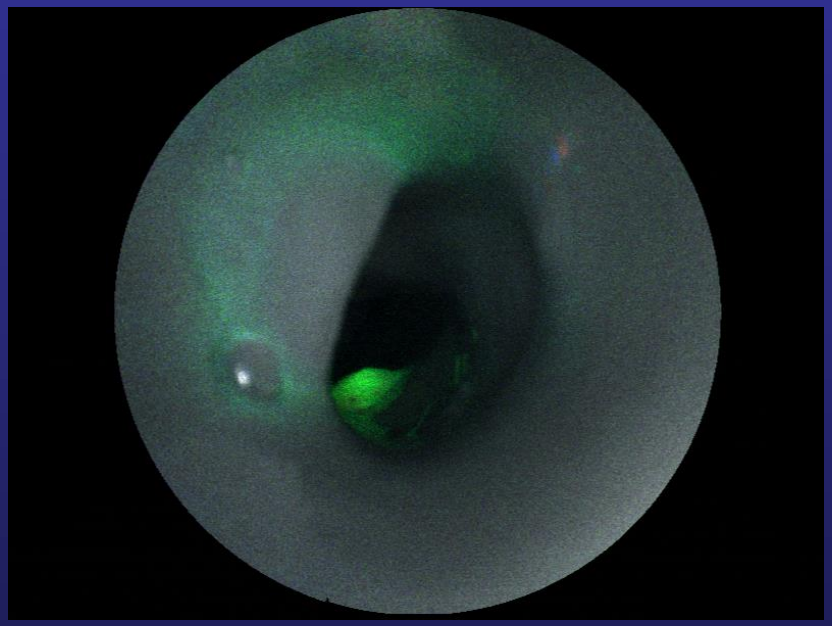
Multispectral (RGB dye) fluorescence



Karl Storz veterinary rigid scope used to find polyps and clean the mouse colon.
Peptides (ErbB2/EGFR/CLDN-1) sprayed, 300 microMolar in 0.5 ml/each, 1.5 ml total.
After 5 minutes incubation and water rinsing, 2.1-mm multispectral SFE scope used.

Endoscopic imaging challenges

- Uniform labeling
- Non-specific binding
- Lack of quantification
  - Distance confounder
  - Spectral overlap:
    - Color mixing
    - Autofluorescence
    - Environment
  - Photobleaching
- No digital record



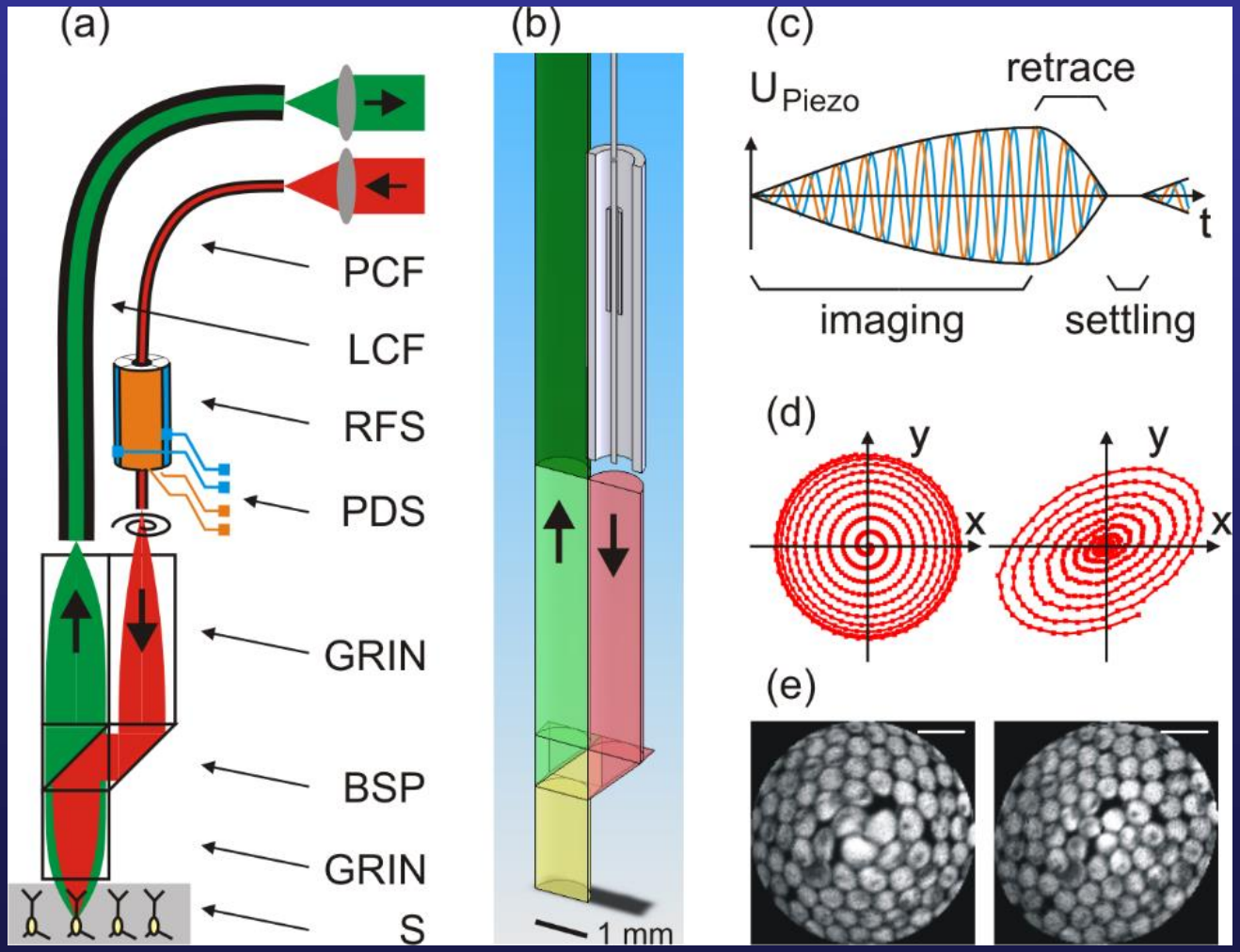
In vivo mouse colon

Arlene Smith U Michigan May 2015

3D SFE Imaging

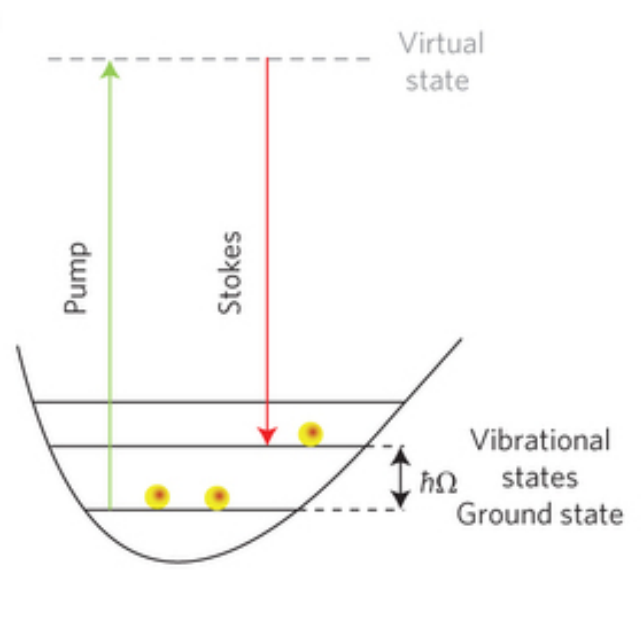
SFE video-rate 2-photon fluorescence

PSF (FWHM) is 1.0 micron laterally and 7.7 microns axially
video rate calcium-indicator mapping of mouse brain activity (0.6 grams in situ)

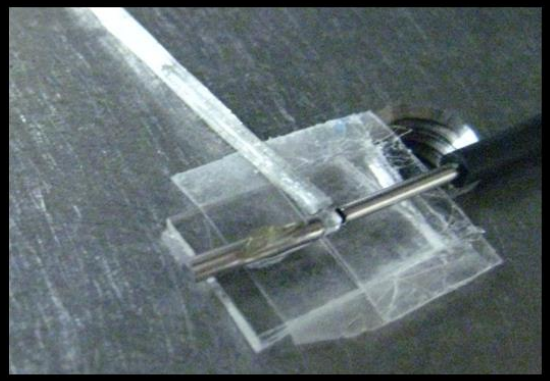


Engelbrecht et al., Optics Express 2008

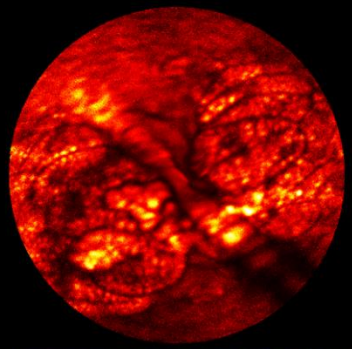
SFE with Raman/CARS contrast lipid imaging

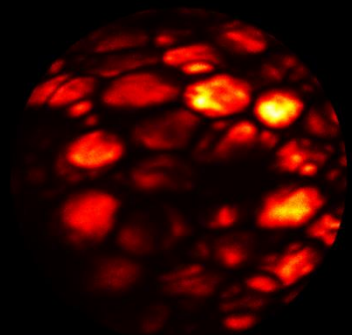


Tip diameter: 1.4 mm

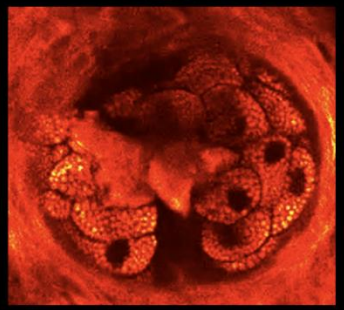


endoscope 0.3 NA

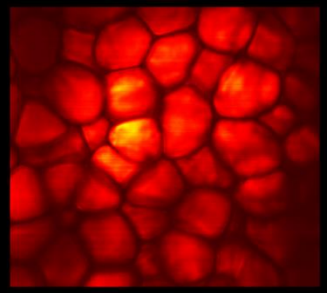




CARS microscope 1.1 NA



sebaceous gland

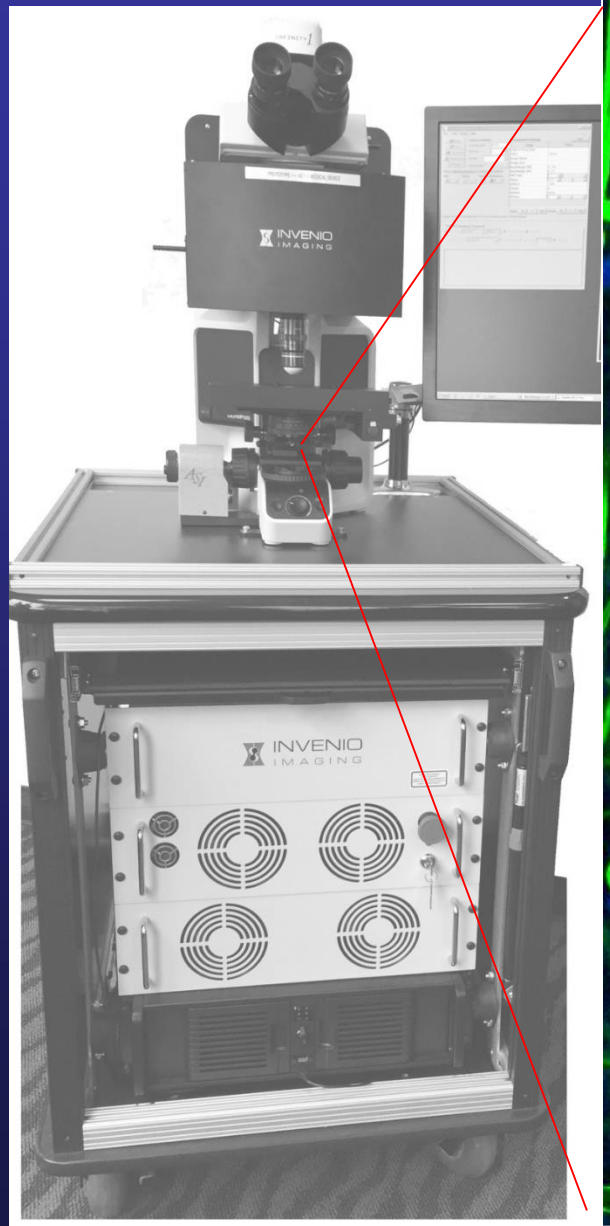


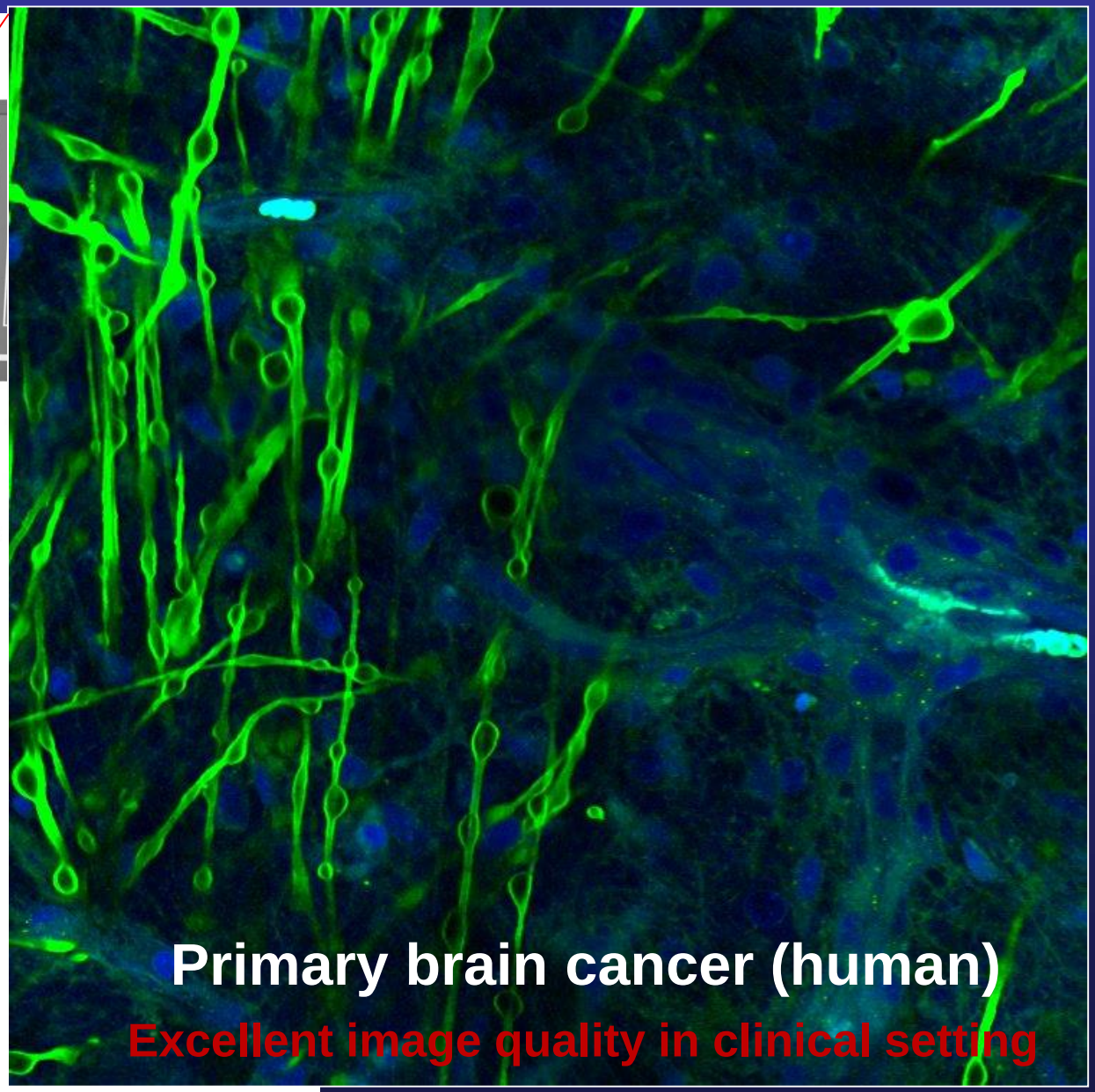
subcutaneous fat

Similar to Englebrecht *et al. Opt. Exp.* 16, 5556, **2008**.

Saar, Optics Letters 2011

Stimulated Raman Scattering Microscopy

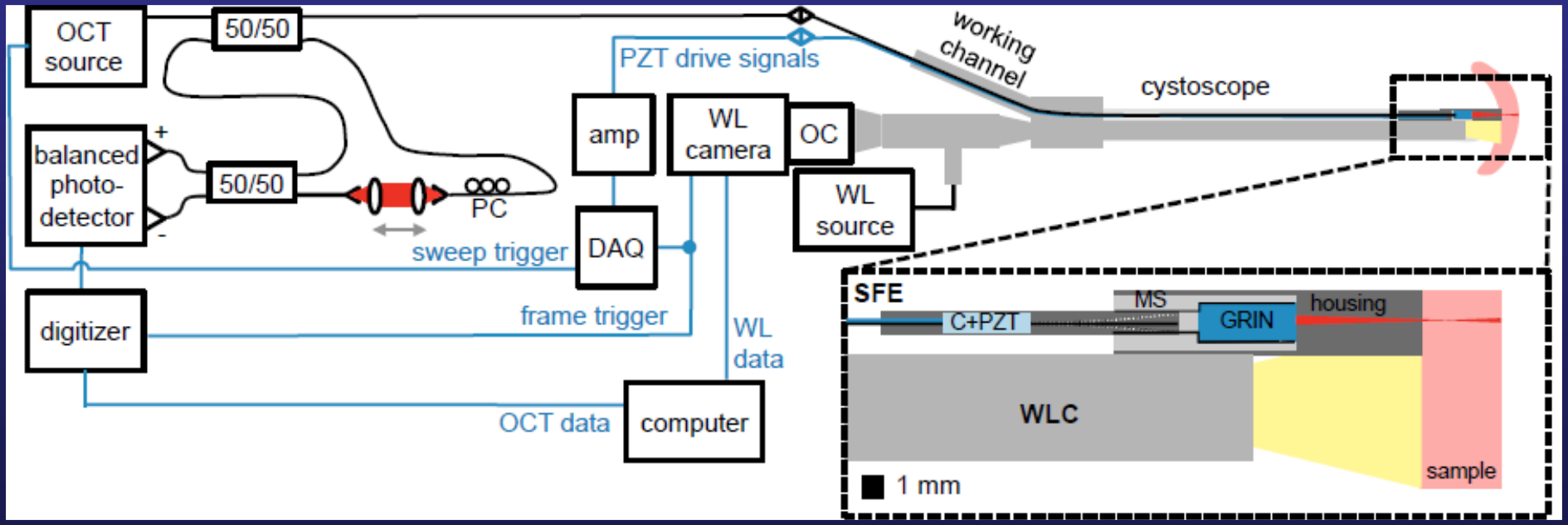




SFE optical scattering contrast
Optical Coherence Tomography (OCT)

3D optical imaging with mosaicking to increase imaged field

In collaboration with Professor Audrey Ellerbee, Stanford University



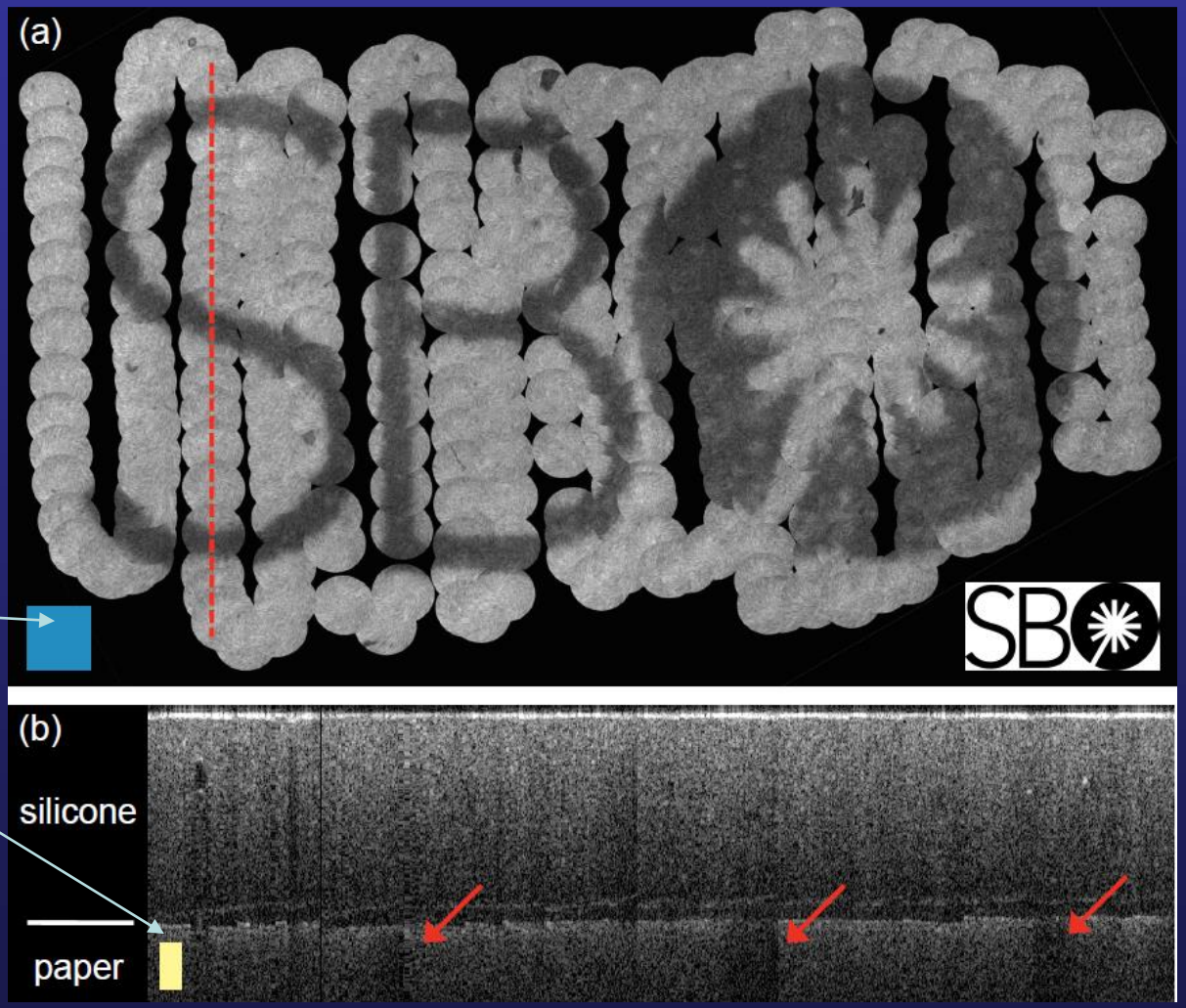
Lurie et al., Optics Letters 2015

Optical Coherence Tomography (OCT)

OCT Mosaic
10 x 20 mm
Summed
Voxel
Projection

1.0 mm ^{2}

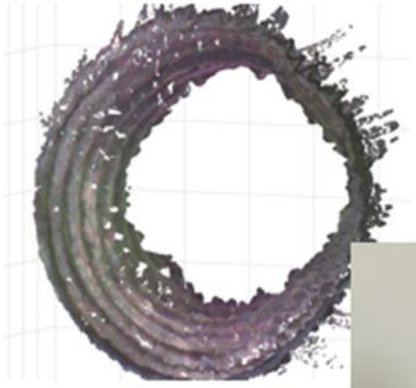
0.2 mm
depth



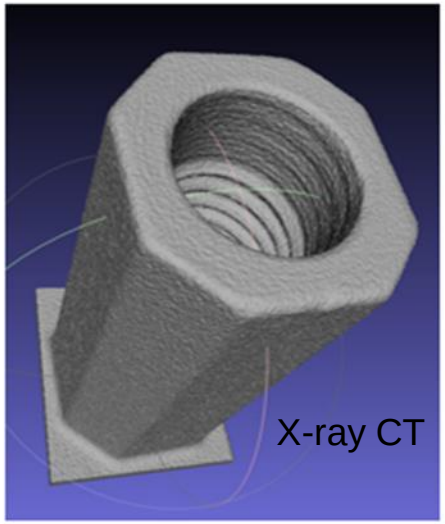
Lurie et al., Optics Letters 2015 – red arrows indicate ink on paper along red dashed line

3D optical metrology with SFE & robot

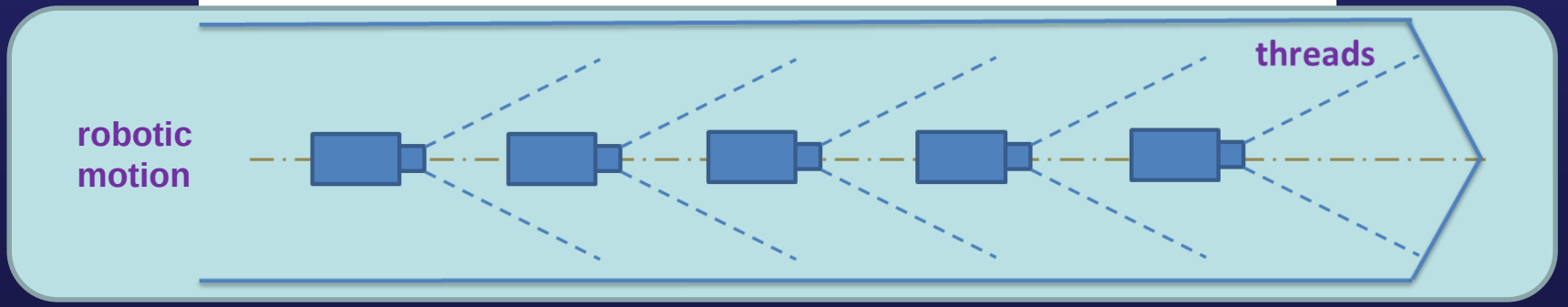
Reconstructed image from 2 SFE frames



M8 threaded hole
7-mm inner diameter



3D X-ray to 3D optical
0.4-mm average error

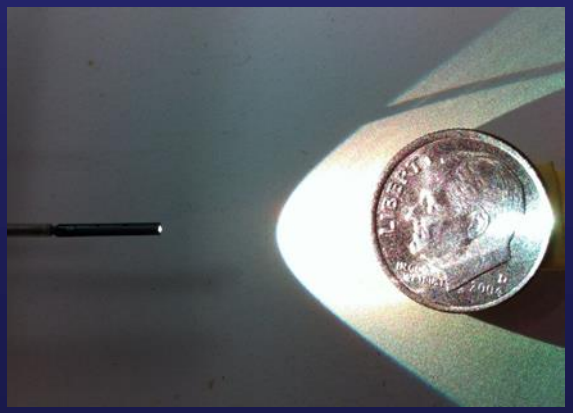


Gong et al., Intl. J. Optomechatronics 2015 – Axial Stereo Application

Conclusions

SFE – A versatile, new fiber endoscope technology

- Highest image resolution for small size
- Forward-viewing to guide interventions
- Wide bandwidth (UV-visible-NIR-SWIR)
- Multimodal in 2D (reflectance & fluorescence)
- Integrated diagnosis and spectroscopy
- 3D imaging (two-photon fluor., Raman, & OCT)
- Disposable scope and tools
- Record and reconstruct
  for quantitative analysis
- Future: multimodal in 3D
  with mosaicking



Demonstrated SFE Performance

	SFE Spec
Rigid Tip Diameter [mm]	≥1.0
Rigid Tip Length [mm]	8-10
Shaft Length [m]	4.3
Viewing Direction	Forward / Side demonstrated
Field of View [deg]	≤110 (air)
Resolution (microns)	1-50 (600 lines)
Depth of Field [mm]	2-50 (low NA lens)
Frame Rate [Hz]	30 @ 600 lines resolution
Image quality	Low distortion
Image Modes	RGB, Fluor, 2 Photon, CARS, Confocal, OCT
Use Testing	In Vivo Animal + Human

Contact for additional information

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Human Photonics Lab

Collaborators – Thank you!

Tom Wang, Univ. of Michigan
Brian Wilson, Univ. Toronto
Fritjof Helmchen, Univ. Zurich
Sunney Xie, Harvard
Audrey Ellerbee, Stanford
INO (Quebec), Invenio-Imaging (CA), VerAvanti (WA)

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